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NEWS 36 Dec 17 TOXCENTER enhanced with additional content
NEWS 37 Dec 17 Adis Clinical Trials Insight now available on STN
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=> s parkin or parkin2
L1 822 PARKIN OR PARKIN2

=> s l1 and (transgen? or knockout or knock out or delet? or deficien?)
L2 172 L1 AND (TRANSGEN? OR KNOCK OUT OR KNOCKOUT OR DELET? OR DEFICIEN
?)

=> s parkin2
L3 1 PARKIN2

=> d bib abs 1-
YOU HAVE REQUESTED DATA FROM 1 ANSWERS -
CONTINUE? Y/(N) y

L3 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2003 ACS
AN 2001:167694 CAPLUS
DN 134:203465
TI Mouse ***parkin2*** cDNA and protein sequences for a transgenic animal model of Parkinson's and neurodegenerative diseases
IN Lubbert, Hermann
PA Biofrontera Pharmaceuticals G.m.b.H., Germany
SO Eur. Pat. Appl., 62 pp.
CODEN: EPXXDW
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI EP 1081225	A1	20010307	EP 1999-116766	19990830
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, L, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
WO 2001016176	A2	20010308	WO 2000-EP8071	20000818
WO 2001016176	A3	20010927		
W: CA, JP, US				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
EP 1208200	A2	20020529	EP 2000-956461	20000818
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, L, LU, NL, SE, MC, PT, IE, FI, CY				
PRAI EP 1999-116766	A	19990830		
WO 2000-EP8071	W	20000818		

AB This patent application claims mouse gene mPark2 (***parkin2***) nucleotide and protein sequences with mutations or deletions which correspond to mutations in the human gene PARK2 (***parkin2***) sequences that cause Parkinson's disease. The application claims use of polynucleotide and protein sequences for diagnosis. The application also claims the construction of a transgenic non-human animal contg a mutated

DNA sequence and therefore expressing no or a less active or non-active
parkin protein. The patent application further claims use of transgenic
animals as a model for neurodegenerative diseases. The transgenic animals
can be used for screening therapeutic agents, evaluating treatments, and
examg. disease pathol., and bred for other studies.
RE.CNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD
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=> s park2
L4 54 PARK2

=> dup rem l4
PROCESSING COMPLETED FOR L4
L5 32 DUP REM L4 (22 DUPLICATES REMOVED)

=> s l5 and (transgen? or knockout or knock out or delet? or deficien?)
L6 13 L5 AND (TRANSGEN? OR KNOCKOUT OR KNOCK OUT OR DELET? OR DEFICIE
N?)

=> d bib abs 1-
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L6 ANSWER 1 OF 13 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC
AN 2002:389444 BIOSIS
DN PREV200200389444
TI Molecular findings in familial Parkinson disease in Spain.
AU Hoenicka, Janet (1); Vidal, Lidice; Morales, Blas; Ampuero, Israel;
Jimenez-Jimenez, F. Javier; Berciano, Jose; del Ser, Teodoro; Jimenez,
Adriano; Ruiz, Pedro G.; de Yebenes, Justo G.
CS (1) Banco de Tejidos para Investigaciones Neurologicas, Facultad de
Medicina, Universidad Complutense de Madrid, Avda. Complutense s/n,
Pabellon III, Sotano, Madrid, 28040, jhoenicka@cbm.uam.es, Spain
SO Archives of Neurology, (June, 2002) Vol. 59, No. 6, pp. 966-970.
http://www.archneurol.com, print.
ISSN: 0003-9942.
DT Article
LA English
AB Background: Several genetic errors in alpha-synuclein (Park1) and
ubiquitin carboxyl-terminal-hydrolase L1(Park5) genes cause autosomal
dominant familial Parkinson disease. Mutations in the parkin gene (
Park2) are the major cause of autosomal recessive Parkinson
disease. Objective: To analyze the clinical and molecular data of 19
Spanish kindreds (13 with recessive, 4 with dominant, and 2 with uncertain
inheritance) who have familial Parkinson disease. Methods: We searched for
the previously described mutations in Park1 and Park5 genes and for new or
described mutations in ***Park2***. We used single-strand conformation
polymorphism, direct sequencing, and restriction digestion of polymerase
chain reaction (PCR)-amplified genomic DNA for this study. Results: None
of these families have either Park1 or Park5 mutations. We found 5
different mutations in ***Park2*** gene in 5 of the families with
recessive inheritance. To our knowledge, 2 of these mutations, V56E and
C212Y, have not been previously reported. The other mutations found (
deletion of exons 3 and 5 and 225delA) have been described in
other ethnic groups. Heterozygous carriers of a single ***Park2***
mutation either were asymptomatic or developed clinical symptoms in late
adulthood or after brief exposure to haloperidol therapy. Conclusions:
Mutations in ***Park2*** gene account for 38% of the families with
recessive parkinsonism in Spain. We found 2 cases of simple heterozygous
Park2 mutation carriers that developed clinical symptoms either
in late adulthood or after brief exposure to parkinsonizing agents. Thus,
hereditary Parkinson disease has more variable clinical phenotype and
molecular defects than previously thought since heterozygous mutations
could be a risk factor for parkinsonism.

L6 ANSWER 2 OF 13 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC
AN 2000:495715 BIOSIS
DN PREV200000495836
TI Autosomal recessive early-onset parkinsonism with diurnal fluctuation:
Clinicopathologic characteristics and molecular genetic identification.
AU Yamamura, Yasuhiro (1); Hattori, Nobutaka; Matsumine, Hiroto; Kuzuhara,
Shigeki; Mizuno, Yoshikuni
CS (1) Institute of Health Sciences, Hiroshima University School of Medicine,
Kasumi 1-2-3, Minami-ku, Hiroshima, Japan
SO Brain & Development, (September, 2000) Vol. 22, No. Supplement 1, pp.
S87-S91. print.
ISSN: 0387-7604.
DT Article
LA English
SL English
AB Autosomal recessive early-onset parkinsonism with diurnal fluctuation
(AR-EPDF, syn. autosomal recessive juvenile parkinsonism, ***PARK2***)
is one of the hereditary parkinsonian syndromes. We examined subjects
consisting of 43 patients from 22 families with AR-EPDF. The clinical
features were relatively homogeneous, including the average age at onset
of 26.1 years, beginning with dystonic gait disturbance, diurnal
fluctuation of the symptoms (sleep benefit) unrelated to medication,
dystonia (mainly foot dystonia), hyperactive tendon reflex, remarkable
effect of levodopa and other antiparkinsonism drugs, susceptibility to
dopa-induced dyskinesia, mild autonomic symptoms, absence of dementia, and
slow progression of disease. Some patients had hysteric character or
psychic symptoms provoked by medication. Pathologic study revealed
neuronal loss in the substantia nigra pars compacta and locus coeruleus
without Lewy body formation. We performed extensive molecular genetic
analysis of the parkin gene in 16 families to identify a total of six
different ***deletional*** mutations. In AR-EPDF, loss of newly
discovered 'Parkin' protein is responsible for selective degeneration of
the pigmented neurons in the substantia nigra and locus coeruleus.
Compared with autosomal dominant Parkinson's disease, AR-EPDF appears to
be more prevalent and present in several ethnic groups.

L6 ANSWER 3 OF 13 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC
AN 2000:362925 BIOSIS
DN PREV200000362925
TI Parkin ***deletions*** in a family with adult-onset, tremor-dominant
parkinsonism: Expanding the phenotype.
AU Klein, Christine; Pramstaller, Peter P.; Kis, Bernhard; Page, Curtis C.;
Kann, Martin; Leung, Joanne; Woodward, Heather; Castellan, Claudio C.;
Scherer, Monika; Vieregge, Peter; Breakefield, Xandra O.; Kramer, Patricia
L.; Ozelius, Laurie J. (1)
CS (1) Molecular Genetics, AECOM, 1300 Morris Park Avenue, Bronx, NY, 10461,
USA
SO Annals of Neurology, (July, 2000) Vol. 48, No. 1, pp. 65-71. print.
ISSN: 0364-5134.
DT Article
LA English
SL English

AB A gene for autosomal recessive parkinsonism, ***PARK2*** (parkin), has
recently been identified on chromosome 6q and shown to be mutated in
Japanese and European families, mostly with early onset parkinsonism. Here
we present a large pedigree from South Tyrol (a region of northern Italy)
with adult-onset clinically typical tremor-dominant parkinsonism of
apparently autosomal dominant inheritance. Haplotype analysis excluded
linkage to the chromosome 2p, 4p, and 4q regions that harbor genes
associated with autosomal dominant parkinsonism, but implicated the parkin
locus on chromosome 6q. Compound heterozygous ***deletions*** in the
parkin gene (one large and one truncating) were identified in 4 affected
male siblings. The patients were clinically indistinguishable from most
patients with idiopathic Parkinson's disease. None of them displayed any
of the clinical hallmarks described in patients with previously reported
parkin mutations, including diurnal fluctuations, benefit from sleep, foot
dystonia, hyperreflexia, and early susceptibility to levodopa-induced
dyskinesias. Two affected female individuals carried one (truncating) of
the two ***deletions*** in a heterozygous state with an apparently
normal allele. We conclude that the phenotypic spectrum associated with
mutations in the parkin gene is broader than previously reported,
suggesting that this gene may be important in the etiology of the more
frequent late-onset typical Parkinson's disease.

L6 ANSWER 4 OF 13 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC
AN 1999:227164 BIOSIS
DN PREV199900227164
TI A wide variety of mutations in the parkin gene are responsible for
autosomal recessive parkinsonism in Europe.
AU Abbas, Nacer; Lucking, Christoph B.; Ricard, Sylvain; Durr, Alexandra;
Bonifati, Vincenzo; De Michele, Giuseppe; Bouley, Sandrine; Vaughan, Jenny
R.; Gasser, Thomas; Marconi, Roberto; Broussolle, Emmanuel;
Brefel-Courbon, Christine; Harhangi, Biswadjiet S.; Oostra, Ben A.;
Fabrizio, Edito; Bohme, Georg A.; Pradier, Laurent; Wood, Nick W.; Filla,
Alessandro; Meco, Giuseppe; Denefle, Patrice; Agid, Yves; Brice, Alexis;
(1); French Parkinson's Disease Genetics Study Group; European Consortium
on Genetic Susceptibility in Parkinson's Disease
CS (1) INSERM U289, Hopital de la Salpetriere, 47 Boulevard de l'Hopital,
75651, Paris Cedex 13, France
SO Human Molecular Genetics, (April, 1999) Vol. 8, No. 4, pp. 567-574.
ISSN: 0964-6906
DT Article
LA English
SL English
AB Autosomal recessive juvenile parkinsonism (AR-JP, ***PARK2***, OMIM
602544), one of the monogenic forms of Parkinson's disease (PD), was
initially described in Japan. It is characterized by early onset (before
age 40), marked response to levodopa treatment and levodopa-induced
dyskinesias. The gene responsible for AR-JP was recently identified and
designated parkin. We have analysed the 12 coding exons of the parkin gene
in 35 mostly European families with early onset autosomal recessive
parkinsonism. In one family, a homozygous ***deletion*** of exon 4
could be demonstrated. By direct sequencing of the exons in the index
patients of the remaining 34 families, eight previously undescribed point
mutations (homozygous or heterozygous) were detected in eight families
that included 20 patients. The mutations segregated with the disease in
the families and were not detected on 110-166 control chromosomes. Four
mutations caused truncation of the parkin protein. Three were frameshifts
(202-203delAG, 255delA and 321-322insGT) and one a nonsense mutation
(Trp453Stop). The other four were missense mutations (Lys161Asn,
Arg256Cys, Arg275Trp and Thr415Asn) that probably affect amino acids that
are important for the function of the parkin protein, since they result in
the same phenotype as truncating mutations or homozygous exon
deletions. Mean age at onset was 38 + 12 years, but onset up to
age 58 was observed. Mutations in the parkin gene are therefore not
invariably associated with early onset parkinsonism. In many patients, the
phenotype is indistinguishable from that of idiopathic PD. This study has
shown that a wide variety of different mutations in the parkin gene are a
common cause of autosomal recessive parkinsonism in Europe and that
different types of point mutations seem to be more frequently responsible
for the disease phenotype than are ***deletions***.

L6 ANSWER 5 OF 13 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC
AN 1999:196872 BIOSIS
DN PREV199900196872
TI Chromosome 6-linked autosomal recessive early-onset Parkinsonism: Linkage
in European and Algerian families, extension of the clinical spectrum, and
evidence of a small homozygous ***deletion*** in one family.
AU Tassin, Johann; Durr, Alexandra; de Broucker, Thomas; Abbas, Nacer;
Bonifati, Vincenzo; De Michele, Giuseppe; Bonnet, Anne-Marie; Broussolle,
Emmanuel; Pollak, Pierre; Vidailhet, Marie; De Mari, Michele; Marconi,
Roberto; Medjbeur, Soraya; Filla, Allessandro; Meco, Giuseppe; Agid, Yves;
Brice, Alexis (1); The French Parkinson's Disease Genetics Study Group;
The European Consortium on Genetic Susceptibility in Parkinson's Disease
CS (1) INSERM U289, Hopital de la Salpetriere, 47 bd de l'Hopital, 75651,
Paris Cedex 13, France
SO American Journal of Human Genetics, (July, 1998) Vol. 63, No. 1, pp.
88-94.
ISSN: 0002-9297
DT Article
LA English
AB The gene for autosomal recessive juvenile Parkinsonism (AR-JP) recently
has been mapped to chromosome 6q25.2-27 in Japanese families. We have
tested one Algerian and 10 European multiplex families with early-onset
Parkinson disease for linkage to this locus, with marker D6S305.
Homogeneity analysis provided a conditional probability in favor of
linkage of > 9 in eight families, which were analyzed further with eight
micro-satellite markers spanning the 17-cM AR-JP region. Haplotype
reconstruction for eight families and determination of the smallest region
of homozygosity in two consanguineous families reduced the candidate
interval to 11.3 cM. If the ***deletion*** of two microsatellite
markers (D6S411 and D6S155C) that colocalize on the genetic map and that
segregate with the disease in the Algerian family is taken into account,
the candidate region would be reduced to <1 cM. These findings should
facilitate identification of the corresponding gene. We have confirmed
linkage of AR-JP in European families and in an Algerian family to the
PARK2 locus. ***PARK2*** appears to be an important locus for

AR-JP in European patients. The clinical spectrum of the disease in our
families, with age at onset ltoreq58 years and the presence of painful
dystonia in some patients, is broader than that reported previously.

L6 ANSWER 6 OF 13 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
AN 1998:228246 BIOSIS
DN PREV199800228246
TI A microdeletion of D6S305 in a family of autosomal recessive juvenile
parkinsonism (***PARK2***
AU Matsumine, Hiroto (1); Yamamura, Yasuhiro; Hattori, Nobutaka; Kobayashi,
Tomonori; Kitada, Tohru; Yoritaka, Asako; Mizuno, Yoshikuni
CS (1) Dep. Neurol., Juntendo Univ. Sch. Med., 2-1-1 Hongo, Bunkyo, Tokyo 113,
Japan
SO Genomics, (April 1, 1998) Vol. 49, No. 1, pp. 143-146.
ISSN: 0888-7543.
DT Article
LA English
AB A gene for autosomal recessive juvenile parkinsonism (ARJP; HGMW-approved
symbol ***PARK2***; MIM 600116) has recently been mapped to a 1.7-cM
interval on chromosome 6q25.2-q27. We here report an inbred family with
ARJP showing a perfect cosegregation with null allele for D6S305, which is
a marker within the ARJP locus. We assigned the ***deletion*** within
an interval between D6S1937 and AFMa155td9, which are 0 cM apart from each
other and located on a single YAC clone. Two possibilities should be
evaluated: (1) the ***deletion*** is polymorphic and linked to ARJP,
and (2) the ***deletion*** is pathogenic and contains both D6S305 and
the ARJP gene (or a part of it). An exon search in a ***deleted***
segment or in the relatively small-sized genomic clones harboring D6S305
may enormously facilitate the cloning procedure of the ARJP gene.

L6 ANSWER 7 OF 13 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
AN 2002034266 EMBASE
TI Genetic risk factors. Session V summary and research needs.
AU Farrer M.; Richfield E.
CS M. Farrer, Department of Neuroscience, Center for Neuroscience, Mayo
Clinic, Jacksonville, FL 32224, United States.
farrer.matthew@mayo.edu
SO NeuroToxicology, (2001) 22/6 (845-848).
Refs: 23
ISSN: 0161-813X. CODEN: NRTXDN.
PUI S 0161-813X(01)00087-0
CY Netherlands
DT Journal; Conference Article
FS 008 Neurology and Neurosurgery
022 Human Genetics
037 Drug Literature Index
LA English
SL English
AB The interaction between genetic predisposition, environmental exposure,
and age are well recognized in contributing to human Parkinsonism.
However, the relative importance of each of those factors in any given
case is difficult to ascertain. This session was devoted toward
identifying and exploring genetic risk factors in contributing to human
Parkinsonism. Clues arising from cases with familial Parkinsonism are
proving useful in identifying the biochemical pathways perturbed in
idiopathic Parkinson's disease. Genetic risk factors are identified in
families through a variety of methods. Once a specific gene is identified,
a variety of tools can be used to understand the role of a particular
mutation or possible roles for the wild-type form of the protein in
contributing to human Parkinsonism. This session had three presentations.
the first presentation dealt with identifying genes in human Parkinson's
disease and exploring their functional effects. The second presentation
examined the use of ***transgenic*** mouse models for understanding
the role of gene products in developing Parkinson's disease and how those
models may be used for the development of new treatments. The final talk
examined the role of mitochondrial abnormalities leading to electron
transport deficits in Parkinson's disease and how genes and the
environment may interact. The final talk also examined potential
interventions that may help alleviate functional deficits related to
mitochondrial impairments. Role of Genes in Parkinson's Disease Dr.
Matthew Farrer detailed the search for familial mutations that contribute
to Parkinsonism. He opened his presentation by highlighting the difficulty
in proving a role for environmental exposures in disposing to idiopathic
Parkinson's disease. To date, rural living, well water consumption,
smoking and caffeine intake most reliably have an effect on risk. However,
in many studies the effects are small and confidence intervals may overlap
1.0. Thus, despite intensive epidemiological study the field has been left
with little direction. That is, until now, Farrer highlighted the rapid
pace of identification of genetic mutations contributing to different
types of Parkinsonism. Currently, at least eight genetic loci (Park 1
through Park 8) are known (see Farrer et al., 1999a,b; Polymeropoulos,
1997; Kitada, 1998; Periquet et al., 2001; Gasser, 1998; Leroy, 1998a,b;
Hutton, 1998; Kruger, 1998; Spillantini et al., 1998; Sveinbjornsdottir,
2000; Van Duijn et al., 2001; Valente et al., 2001; Masliah et al., 2001;
Hsu et al., 2000; Takeda et al., 2000; Haas et al., 2001; Shults et al.,
1995, 1997, 1998, 1999; Haas et al., 1995). Park 1, is an autosomal
dominant locus at 4q21 originally described in the Contursi kindred, in
1997, affected individuals were shown to harbor an A1a53Thr mutation in
the alpha-synuclein gene. In 1998, an A1a30Pro alpha-synuclein
mutation was subsequently found in a family of German origin. Many other
talks during this meeting focused on the mechanism of action and roles for
alpha.-synuclein in contributing to idiopathic Parkinson's disease.
Recessively inherited juvenile and early onset Parkinsonism may be due to
Park 2 mutations. The gene affected is located at the tip of chromosome
6q25.2-q27 and encodes Parkin, a novel E3 protein ligase. Less emphasis
was placed on Parkin mutations at this meeting, although their role in
both juvenile Parkinsonism without Lewy body pathology and now later-onset
seemingly sporadic disease is becoming better understood. Mutations
probably account for around 50% of familial, recessive Parkinsonism with
onset <45 years and 18% of seemingly sporadic cases. Parks 3 and 4 have
been mapped in rare families with dominant inheritance patterns, albeit
with reduced penetrance for disease. Park 3 has onset typical for sporadic
Parkinson's disease, and is located at 2p13. Park 4 implicates a genetic
mutation in early onset Parkinsonism-dementia on chromosome 4p15. For Park
5, located at 4p14, the inheritance pattern is unclear although both
Ile93Met and Met124Leu ubiquitin carboxyterminal hydrolyze (UCHL1)
mutations have been implicated in familial disease and a Ser18Tyr
polymorphism is inversely associated with risk for sporadic disease. Parks
6 and 7 are recessive and located at 1p35-p36 and 1p36, respectively. Both
regions were mapped in consanguineous kindreds with relatively early onset

Parkinson's disease and Park 6 like Park 2 may account for disease in multiple families. Chromosome 1p32 has been recently mapped in the Icelandic population to late-onset Parkinson's disease and has tentatively been assigned as Park 8. Dr. Farrer went on to present data outlining the mechanism of action for some of these proteins implicated by genetic studies and how the mutations may predispose to Parkinson's disease. He emphasized the need and importance of further functional studies, presently in their infancy, to elucidate common pathways likely to be perturbed in both familial and sporadic Parkinson's disease. Cellular and animal models, now possible to create, are providing a new generation of research tools. Only on this background can hypotheses about the effects of common environmental agents be tested. Molecular knowledge and models will facilitate the development of novel interventions and rational drug design. By way of analogy, Farrer alluded to the tremendous success this approach has made in Alzheimer's disease. Dr. Farrer presented a web-site address for his work where investigators may obtain these new genetic research tools. Cloned wild-type and mutant genes that cause familial Parkinsonism can be ordered directly from the web-site. There are no restrictions on use and they are available at no cost to academic investigators. The web-site address is www.mayo.edu/fpd/. An effort presently supported by both NINDS and the Mayo Foundation. This site contains recent information about both the Mayo Clinic Jacksonville research efforts. It also contains links to other sites related to Parkinson's disease.

L6 ANSWER 8 OF 13 CAPLUS COPYRIGHT 2003 ACS
AN 2002:965737 CAPLUS
TI Parkin mutations (***Park2***)
AU Mizuno, Yoshikuni; Hattori, Nobutaka; Yoshino, Hiroyo; Asakawa, Shiuchi; Minoshima, Shinsei; Shimizu, Nobuyoshi; Suzuki, Toshiaki; Chiba, Tomoki; Tanaka, Keiji
CS Department of Neurology, Juntendo University School of Medicine, Tokyo, 113-8421, Japan
SO Genetics of Movement Disorders (2003), 305-314. Editor(s): Pulst, Stefan-M. Publisher: Academic Press: San Diego, Calif.
CODEN: 69DIVT. ISBN: 0-12-566652-7
DT Conference
LA English
AB ***Park2*** (autosomal recessive-juvenile parkinsonism, AR-JP) presents young-onset parkinsonism, consisting of gait disturbance, rest tremor, cogwheel rigidity, and bradykinesia. Clin. features are essentially similar to those of late-onset sporadic Parkinson's disease. They respond to levodopa well. Progression is slow. Pathol. features include extensive nigral and locus coeruleus degeneration and gliosis without Lewy body formation. The disease gene has been identified and named parkin, which is located on the long arm of chromosome 6 at 6q25-27.2. Varieties of ***deletion*** mutations and point mutations of parkin have been found in patients with ***Park2***. Also, compd. heterozygotes were found. Parkin protein functions as a ubiquitin ligase and a no. of candidate substrates for Parkin have been reported including CDCrel-1, alpha-synuclein, 22. Pael receptor, synphilin-1, and CDCrel-2A. Accumulation of one or more of the candidate substrates appears to be the cause of nigral degeneration. ***Transgenic*** and ***knock*** - ***out*** animals of parkin have not been reported in the literature. ***Park2*** has been considered to represent the most common form of familial Parkinson's disease. (c) 2003 Academic Press
RE.CNT 59 THERE ARE 59 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 9 OF 13 CAPLUS COPYRIGHT 2003 ACS
AN 2001:517915 CAPLUS
DN 136:245209
TI Analysis of genetic mutation in the 6q25.3 region in breast cancer
AU Hirano, Akira; Utada, Takahito; Nagai, Hisao; Haga, Shunsuke; Kajiwara, Tetsuro; Kasumi, Fujio; Sakamoto, Goi; Nakamura, Yusuke; Emi, Mitsuru
CS Affiliated Second Hospital, Department of Surgery, Tokyo Women's Medical College, Arakawa-ku, Tokyo, 116-8567, Japan
SO Nyugan Kiso Kenkyu (2001), 10, 27-30
CODEN: NKKEFA. ISSN: 1343-2028
PB Nyugan Kiso Kenkyukai
DT Journal
LA Japanese
AB Chromosomal ***deletion*** in breast cancer is analyzed by loss of heterozygosity. Loss of heterozygosity anal. reveals the commonly ***deleted*** region on chromosome 6 in breast cancer and detailed ***deletion*** mapping of chromosome 6 identifies 34 exons within the region. One of the exons perfectly matches with the exon 9 of the ***PARK2*** gene for parkinsonism, indicating the presence of the ***PARK2*** gene at chromosome 6q25.3. These results demonstrate the possible role of the ***PARK2*** gene as a tumor suppressor gene in breast cancer.

L6 ANSWER 10 OF 13 CAPLUS COPYRIGHT 2003 ACS
AN 2001:487635 CAPLUS
DN 136:83991
TI Parkin gene causing benign autosomal recessive juvenile parkinsonism
AU Nisipeanu, P.; Inzelberg, R.; Mouch, S. Abo; Carasso, R. L.; Blumen, S.; Zhang, J.; Matsumine, H.; Hattori, N.; Mizuno, Y.
CS Department of Neurology, Hillel Yaffe Medical Center, Hadera 38100, Israel
SO Neurology (2001), 56(11), 1573-1575
CODEN: NEURAI. ISSN: 0028-3878
PB Lippincott Williams & Wilkins
DT Journal
LA English
AB Autosomal recessive juvenile parkinsonism (AR-JP) is an early-onset parkinsonism caused by exonic ***deletions*** or point mutations in the parkin gene. The relationship between the type of the genetic defect and the clin. presentation, the response to therapy, and the evolution have not been yet detd. The authors describe a single-basepair ***deletion*** at nucleotide 202 in exon 2 of the parkin gene in a kindred with a benign clin. course.
RE.CNT 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 11 OF 13 CAPLUS COPYRIGHT 2003 ACS
AN 2001:382045 CAPLUS
DN 136:113296
TI Autosomal recessive juvenile parkinsonism (AR-JP): Genetic diagnosis
AU Matsumine, Hiroto; Hattori, Nobutaka; Mizuno, Yoshikuni
CS Department of Neurology, Juntendo University School of Medicine, Tokyo, Japan
SO Methods in Molecular Medicine (2001), 62(Parkinson's Disease), 13-29
CODEN: MMMEFN
PB Humana Press Inc.
DT Journal
LA English
AB The autosomal recessive juvenile parkinosonism (AR-JP) is linked to the 17-cM region on chromosome 6q25.2-27 and the locus is designated

Park2 Parkin is the responsible gene for the disease
Abnormalities in this gene which are specific for AR-JP include
homozygous exonic ***deletions*** small ***deletions*** and
point mutations The presence of homozygous exonic ***deletions***
supports the notion that nigral neurodegeneration in AR-JP is caused by
loss of function of the parkin protein The anal of mutations in the
parkin gene is also presented
RE CNT 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 12 OF 13 CAPLUS COPYRIGHT 2003 ACS
AN 2001:167694 CAPLUS
DN 134:203465
TI Mouse park n2 cDNA and protein sequences for a ***transgenic*** animal
model of Parkinson's and neurodegenerative diseases
IN Lubbert, Hermann
PA Biofrontera Pharmaceuticals G m b H., Germany
SO Eur. Pat. Appl., 62 pp.
CODEN: EPXXDW
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI EP 1081225	A1	20010307	EP 1999-116766	19990830
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
WO 2001016176	A2	20010308	WO 2000-EP8071	20000818
WO 2001016176	A3	20010927		
W: CA, JP, US				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
EP 1208200	A2	20020529	EP 2000-956461	20000818
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY				
PRAI EP 1999-116766	A	19990830		
WO 2000-EP8071	W	20000818		

AB This patent application claims mouse gene mPark2 (parkin2) nucleotide and
protein sequences with mutations or ***deletions*** which correspond
to mutations in the human gene ***PARK2*** (parkin2) sequences that
cause Parkinson's disease The application claims use of polynucleotide
and protein sequences for diagnosis The application also claims the
construction of a ***transgenic*** non-human animal contg. a mutated
DNA sequence and therefore expressing no or a less active or non-active
parkin protein The patent application further claims use of
transgenic animals as a model for neurodegenerative diseases. The
transgenic animals can be used for screening therapeutic agents,
evaluating treatments, and examg disease pathol., and bred for other
studies
RE CNT 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 13 OF 13 CAPLUS COPYRIGHT 2003 ACS
AN 2000:297432 CAPLUS
DN 133:220862
TI Progress in the clinical and molecular genetics of familial parkinsonism
AU Kitada, Tohru; Asakawa, Shuichi; Matsumine, Hiroto; Hattori, Nobutaka;
Shimura, Hideki; Minoshima, Shinsei; Shimizu, Nobuyoshi; Mizuno, Yoshikuni
CS Department of Neurology, Juntendo University School of Medicine, Tokyo,
113-8421, Japan
SO Neurogenetics (2000), 2(4), 207-218
CODEN: NEROFX; ISSN: 1364-6745
PB Springer-Verlag
DT Journal; General Review
LA English

AB A review, with 106 refs. Parkinson's disease (PD) is a neurodegenerative
disease with clin. features resulting from ***deficiency*** of
dopamine in the nigrostriatal system. Most PD cases are sporadic and the
primary cause of the disease is still unknown. Recently, familial PD and
parkinsonism have received much attention because these forms of the
disease might provide clues to the genetic risk factors involved in the
pathogenesis of idiopathic PD. To date, two causative genes,
alpha-synuclein and the parkin gene, have been identified.
Alpha-Synuclein is involved in the pathogenesis of an autosomal dominant
form of PD and constitutes a major component of the Lewy body, which is a
pathol. hallmark of idiopathic PD. In addn., mutations in the parkin gene
have been identified as the cause of autosomal recessive juvenile
parkinsonism (AR-JP). AR-JP manifests itself as a highly selective
degeneration of the substantia nigra and the locus coeruleus, but without
Lewy body formation. In addn. to these two genes, four chromosomal loci
have been linked to other forms of familial PD. Furthermore, there are a
no. of other pedigrees of familial PD in which linkage to known genetic
loci has been excluded. Mol. cloning of these disease genes and
elucidation of the function of their gene products will greatly contribute
to the understanding of the pathogenesis of idiopathic PD.
RE CNT 106 THERE ARE 106 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d his

(FILE 'HOME' ENTERED AT 17:29:29 ON 16 JAN 2003)

FILE 'BIOSIS, EMBASE, CAPLUS' ENTERED AT 17:29:41 ON 16 JAN 2003
L1 822 S PARKIN OR PARKIN2
L2 172 S L1 AND (TRANSGEN? OR KNOCKOUT OR KNOCK OUT OR DELET? OR DEFIC
L3 1 S PARKIN2
L4 54 S PARK2
L5 32 DUP REM L4 (22 DUPLICATES REMOVED)
L6 13 S L5 AND (TRANSGEN? OR KNOCKOUT OR KNOCK OUT OR DELET? OR DEFI

=> dup rem l2
PROCESSING COMPLETED FOR L2
L7 105 DUP REM L2 (67 DUPLICATES REMOVED)

=> s l2 and PY<1999
1 FILES SEARCHED...
L8 22 L2 AND PY<1999

=> d bibabs
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REENTER DISPLAY FORMAT FOR ALL FILES (FILEDEFAULT) abs

L8 ANSWER 1 OF 22 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC
AB Autosomal recessive juvenile parkinsonism (AR-JP) is a distinct clinica
and genetic entity characterized by selective degeneration of nigral
dopaminergic neurons and young-onset parkinsonism with remarkable response
to levodopa. Recently, we mapped the gene locus for AR-JP to chromosome
6q25.2-q27 by linkage analysis and we identified a novel large gene,
Parkin, consisting of 12 exons from this region, mutations of this
gene were found to be the cause of AR-JP in two families. Now we report
results of extensive molecular analysis on 34 affected individuals from 18
unrelated families with AR-JP. We found four different homozygous

intragenic ***deletional*** mutations involving exons 3 to 4 exon 3,
exon 4, and exon 5 in 10 families (17 affected individuals). In addition
to the exonic ***deletions*** we identified a novel one-base
deletion involving exon 5 in two families (2 affected
individuals). All mutations so far found were ***deletional*** types
in which large exonic ***deletion*** accounted for 50% (17 of 34) and
the one-base ***deletion*** accounted for 6% (2/34), in the remaining
no homozygous mutations were found in the coding regions. Our findings
indicate that loss of function of the ***Parkin*** protein results in
the clinical phenotype of AR-JP and that subregions between introns 2 and
5 of the ***Parkin*** gene are mutational hot spots

=> d his

(FILE 'HOME' ENTERED AT 17:29:29 ON 16 JAN 2003)

FILE 'BIOSIS, EMBASE, CAPLUS' ENTERED AT 17:29:41 ON 16 JAN 2003
L1 822 S PARKIN OR PARKIN2
L2 172 S L1 AND (TRANSGEN? OR KNOCKOUT OR KNOCK OUT OR DELET? OR DEFIC
L3 1 S PARKIN2
L4 54 S PARK2
L5 32 DUP REM L4 (22 DUPLICATES REMOVED)
L6 13 S L5 AND (TRANSGEN? OR KNOCKOUT OR KNOCK OUT OR DELET? OR DEFI
L7 105 DUP REM L2 (67 DUPLICATES REMOVED)
L8 22 S L2 AND PY<1999

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WEST Search History

DATE: Thursday, January 16, 2003

Set Name side by side	Query	Hit Count	Set Name result set
DB	*USPT;PGPB;JPAB;DWPI; PLUR YES; OP ADJ*		
L6	l5 and (transgen$ or knockout or knock out or knock-out or delet$ or deficien$)	29	L6
L5	L4 or l2	34	L5
L4	l1 near3 (gene or protein)	17	L4
L3	L2 and (transgen$ or knockout or knock out or knock-out or delet$ or deficien$)	26	L3
L2	l1 and parkinson disease	29	L2
L1	Parkin or parkin2	1958	L1

END OF SEARCH HISTORY